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(54) **METHOD FOR VOLTAGE-GATED PROTEIN FRACTIONATION**

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See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

6,391,937 B1	5/2002	Beuhler
6,673,615 B2	1/2004	Denison
7,005,264 B2	2/2006	Su
7,114,378 B1	10/2006	Barth
2002/0146839 A1	10/2002	Guttman
2005/0034990 A1	2/2005	Crooks
2006/0180469 A1	8/2006	Han
2006/0228717 A1	10/2006	Joyce

OTHER PUBLICATIONS

Martin M. Chui; Ronald J. Phillips; Michael J. McCarthy; "Measurement of the Porous Microstructure of Hydrogels by Nuclear Magnetic Resonance", Journal of Colloid and Interface Science, 1995, vol. 174, pp. 336-344.

Debora Foguel; Gregorio Weber; "Pressure-induced Dissociation and Denaturation of Allophycocyanin at Subzero Temperatures", Journal of Biological Chemistry, 1995, vol. 270, No. 48, pp. 28759-28766.

Ellika U. Weber-Ban; Brian G. Reid; Andrew D. Miranker; Arthur L. Horwich; "Global unfolding of a substrate protein by the Hsp100 chaperone ClpA", Nature, 1999, vol. 401, pp. 90-93.

J. Han; H. G. Craighead; "Separation of Long DNA Molecules in a Microfabricated Entropic Trap Array", Science, 2000, vol. 288, No. 5468, pp. 1026-1029.

Shihai Huang; Kevin S. Ratliff; Andreas Matouschek; "Protein unfolding by the mitochondrial membrane potential," Nature Structural Biology, 2002, vol. 9, No. 4, pp. 301-307.

Jonathan J. Nakane; Mark Akeson; Andre Marziali; "Nanopore sensors for nucleic acid analysis", Journal of Physics: Condensed Matter, 2003, vol. 15, pp. 1365-1393.

(Continued)

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(57) **ABSTRACT**

We report unique findings on the voltage dependence of protein exclusion from the pores of nanoporous polymer exclusion membranes. The pores are small enough that proteins are excluded from passage with low applied electric fields, but increasing the field enables proteins to pass through. The requisite field necessary for a change in exclusion is protein-specific with a correlation to protein size. The field-dependence of exclusion is important to consider for preconcentration applications. The ability to selectively gate proteins at exclusion membranes is also a promising means for manipulating and characterizing proteins. We show that field-gated exclusion can be used to selectively remove proteins from a mixture, or to selectively trap protein at one exclusion membrane in a series.

23 Claims, 7 Drawing Sheets

